Page of 1 of Form PTO-1413 U.S. Department of Commerce (REV. 2-82) Participant Department Office Atty. Docket No. Serial No. AP33710 - 072734.0120 10/006,957 Applicant INFORMATION DISCLOSURE STATEMENT Paglin et al.. BY APPLICANT Filing Date Group (Use several sheets if necessary) December 4, 2001 1623 Examiner Confirmation No. Fischer, Latonia 2771

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	FOREIGN PATENT DOCUMENTS										
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08	54.	WO 90/11364	10/04/90	WIPO	C12P	10/30					

No.	OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)
1.	Boyd MR et al., 2001, "Discovery of a novel antitumor benzolactone enamide class that selectively inhibits mammalian vacuolar-type (H+)-atpases" J. Pharmacology and Experimental Therapeutics 297(1):114-120.
2.	Gingras AC et al., 2001, "Regulation of translation initiation by FRAP/mTOR" Genes and Development 15:807-826.
3.	Murakami T et al., 2001, "Elevated expression of vacuolar proton pump gene and cellular pH in cisplatin resistance" Int. J. Cancer 93:869-874.

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Examiner	X. S.	Date Considered	13 Har 03	

^{*} Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Examiner Fischer, Latonia	Confirmation No 2771			

No.	OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)
4.	Paglin S et al., 2001, "A novel response of cancer cells to radiation involves autophagy and formation of acidic vesicles" Cancer Res. 61:439-444.
5.	Hollister TC et al., Nov. 4-8, 2001, "Vacuolar-proton-ATPase is involved in the response of cancer cells to ionizing radiation and is a new target for radiosensitization", 43rd Annual American Society for Therapeutic Radiology and Oncology (ASTRO).
6.	Xu T et al., 2001, "Microtubules are involved in glucose-dependent dissociation of the yeast vacuolar [H+]-ATPase in vivo", J Biol Chem. 276(27):24855-24861.
7.	Gilles F et al., 2000, "A. MUCI dysregulation as the consequence of a t(1;14)(q21;q32) translocation in an extranodal lymphoma" Blood 95(9):2930-2936.
8.	Kim J et al., 2000, "Autophagy, cytoplasm-to-vacuole targeting pathway, and pexophagy in yeast and mammalian cells", Ann. Rev. Biochem. 69:303-342.
9.	Petiot A et al., 2000, "Distinct classes of phosphatidylinositol 3'-kinases are involved in signaling pathways that control macroautophagy in HT-29 cells" J. Biol. Chem. 275(2):992-998.
10.	Finkel E, 1999, "Does Cancer therapy trigger cell suicide?" Science 286(5448):2256-2258.
11.	Reed J, 1999, "Dysregulation of apoptosis in cancer" J Clin Oncol. 17(9):2941-2953.
12.	Forgac M, 1999, "Structure and properties of the vacuolar (H+) ATPases" J. Biol. Chem. 274(19):12951-12954.
13.	Brown JM et al., 1999, "Apoptosis, p53, and tumor cell sensitivity to anticancer agents" Cancer Research 59:1391-1399.
14.	Thangara M et al., 1999, "Interdependent regulation of intracellular acidification and SHP-1 in apoptosis" Cancer Research 59:1649-1654.

NY02:426567.1					
Examiner	L.X	Date Considered	13	Har 03	

^{*} Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	Examiner Fischer, Latonia	Confirmation No 2771				
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N	OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)
15	Gagliardi S et al., 1999, "Chemistry and structure activity relationships of bafilomycin Al, a potent and selective inhibitor of the vacuolar H+-ATPase" Current Medicinal Chemistry 6(12):1197-1212.
16	Mizushima N et al., 1998, "A new protein conjugation system in human. The counterpart of the yeast Apg12p conjugation system essential for autophagy" J Biol Chem. 273(51):33889-33892.
17.	Mizushima N et al., 1998, "A protein conjugation system essential for autophagy" Nature 395(6700):395-398.
18.	Altan N et al., 1998, "Defective acidification in human breast tumor cells and implications for chemotherapy" J Exp Med. 187(10):1583-1598.
19.	Jänicke RU et al., 1998, "Caspase-3 is required for DNA fragmentation and morphological changes associated with apoptosis" J. Biol. Chem. 273(16):9357-9360.
20.	Noda T et al., 1998, "Tor, a Phosphatidylinositol Kinase Homologue, Controls Autophagy in Yeast" J. Biol. Chem. 273(7):3963-3966.
21.	Hammond EM et al., 1998, "Homology between a human apoptosis specific protein and the product of APG5, a gene involved in autophagy" FEBS Lett. 425:391-395.
22.	Ohta T et al., 1998, "Bafilomycin A1, induces apoptosis in the human pancreatic cancer cell line CAPAN-1" J. Pathology 185:324-340.
23.	Blommaart EFC et al., 1997, "Autophagic proteolysis: control and specificity" Biochem. Journal 29:365-385.
24.	Dröse S et al., 1997, "Bafilomycin and concanamycins as inhibitors of V-ATPases and P-ATPases" J. Exp. Biology 200:1-8.
25. 26-	Jia L et al., 1997, "Inhibition of autophagy abrogates tumour necrosis factor a induced apoptosis in human T-lymphoblastic leukaemic cells" British Journal of Haematology 98:673-685.

NY02:426567.1				
Examiner	Date Considered	13	War 03	

^{*} Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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(Use several sheets if necessary)	Filing Date December 4, 2001	Group 8 1623
	Examiner Fischer, Latonia	Confirmation No. 2771

No.	OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)
26.	Keeling DJ et al., 1997, "Vacuolar (H+)-ATPases. Targets for drug discovery?" Ann. N.Y. Acad Sciences 834:600-608.
27.	Paglin S et al., 1997, "Radiation-induced micronuclei formation in human breast cancer cells: Dependence on serum and cell cycle distribution" Biochem and Biophys Research Communications 237(RC977117):678-684.
28.	Bristow RG et al., 1996, "The p53 gene as a modifier of intrinsic radiosensitivity: implications for radiotherapy" Radiotherapy and Oncology 40:197-223.
29.	Bursch W et al, 1996, "Active cell death induced by the anti-estrogens tamoxifen and ICI 164 384 in human mammary carcinoma cells (MCF-7) in culture: the role of autophagy" Carcinogenesis 17:1595-1607.
30.	Verheij M et al., 1996, "Requirement for ceramide initiated SAPK/JNK signaling in stress-induced apoptosis" Nature 380:75-79.
31.	Bose R et al., 1995, "Ceramide synthase mediates Daunorubicin-induced apoptosis: An alternative mechanism for generating death signals" Cell. 82:405-414.
32.	Boyd MR et al., 1995, "Some practical considerations and applications of the National Cancer Institute in vitro anticancer drug discovery screen" Drug Dev. Res. 34:91-109.
33.	Gottlieb RA et al., 1995, "Cell acidification in apoptosis: granulocyte colony-stimulating factor delays programmed cell death in neutrophils by up-regulating the vacuolar H(+)-ATPase" Proc Natl Acad Sci USA 92:5965-5968.
34.	Lee BS et al., 1995, "Transcriptional regulation of the vacuolar H(+)-ATPase B2 subunit gene in differentiating THP-1 cells" J. Biol. Chem. 270(13):7320-7329.
35.	Zakeri Z et al., 1995, "Cell death: programmed, apoptosis, necrosis, or other?" cell Death and Differentiation 2:87-96.

NY02:42656	7.)			
Examiner	S. S.	Date Considered	13 Nar 03	

^{*} Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Examiner Fischer, Latonia	Confirmation N 2771	lo.	

No.	OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)
John 36.	Bronstein I et al., 1994, "Chemiluminescent reporter gene assays: sensitive detection of the GUS and SEAP gene products" Biotechniques 17(1):172-177.
37.	Haimovitz-Friedman A et al., 1994, "Ionizing radiation acts on cellular membranes to generate ceramide and initiate apoptosis" J. Exp. Med. 180:525-535.
38.	Palokangas H et al., 1994, "Active vacuolar H+ATPase is required for both endocytic and exocytic processes during viral infection of BHK-21 cells" J Biol Chem. 269(26):17577-17585.
39.	Houghton AN et al., 1994, "A Tribute to Zanvil Alexander Cohn, (1926-1993)" J. Exp. Med. 179:1-30.
40.	Traganos F et al. 1994, "Lysosomal proton pump activity: Supravital cell staining with acridine orange differentiates leukocytes subpopulations" Methods in Cell Biology 41:185-194.
41.	Wollman R et al., 1994, "Effect of epidermal growth factor on the growth and radiation sensitivity of human breast cancer cells in vitro" Int J Radiation Oncol Biol Phys. 30(1):91-98.
42.	Manabe T et al., 1993, "Inhibitors of vacuolar-type H(+)-ATPase suppresses proliferation of cultured cells" J. Cell Physiol 157:445-452.
43.	Schwartz LM et al., 1993, "Do all programmed cell deaths occur via apoptosis?" Proc. Natl. Acad Sci. USA 90:980-984.
44.	Songyang Z et al., 1993, "SH2 domains recognize specific phosphopeptide sequences" Cell 72:767-778.
45.	van Hille B et al., 1993, "Identification of two subunit A isoforms of the vacuolar H(+)-ATPase in human osteoclastoma" J. Biol. Chem. 268(10):7075-7080.
46.	Lenk SE et al., 1992, "Ubiquitin-activating enzyme, El, is associated with maturation of autophagic vacuoles" J. Cell Biology 118(2):301-308.
47.	Maher LJ, 1992, "DNA triple-helix formation: an approach to artificial gene repressors?" Bioessays 14(12):807-815.
NY02:426567.1	

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Examiner Date Considered 13 War 09

^{*} Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	Examiner Fischer, Latonia	Confirmation No. 2771		
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No.	OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)
38 .	Metzelaar JM et al., 1992, "Lysosomal membrane glycoproteins in platelets" Thrombosis and Haemostasis 68(4):378-382.
49.	Gillespie GA et al., 1991, "CpG island in the region of an autosomal dominant polycystic kidney disease locus defines the 5' end of a gene encoding a putative proton channel" Proc. Natl. Acad. Sci USA 88:4289-4293.
50.	Hélène C, 1991, "The anti-gene strategy: control of gene expression by triplex-forming-oligonucleotides" <i>Anticancer Drug Des.</i> <u>6</u> :569-584.
51.	Houghten RA et al., 1991, "Generation and use of synthetic peptide combinatorial libraries for basic research and drug discovery" Nature 354:84-86.
52.	Lam KS et al., 1991, "A new type of synthetic peptide library for identifying ligand-binding activity" Nature 354:82-84.
53.	Roberts CJ et al., 1991, "Methods for studying the yeast vacuole" Methods In Enzymol. 194:644-661.
55.	Yeh HI et al., 1991, "Proton accumulation and ATPase activity in Golgi apparatus-enriched vesicles from rat liver" J. Cell Biol. 13(3):523-533.
56.	Yoshimori T et al., 1991, "Bafilomycin A ₁ , a specific inhibitor of vacuolar-type H ⁺ -ATPase, inhibits acidification and protein degradation in lysosomes of cultured cells" J. Biol. Chem. 266(26):17707-17712.
57.	Dunn WA, 1990, "Studies on the mechanisms of autophagy: maturation of the autophagic vacuole" J. Cell Biol. 110:1935-1945.
58.	Sarver N et al., 1990, "Ribozymes as potential anti-HIV-1 therapeutic agents" Science 247:1222-1225.
59.	Wang ZQ et al., 1990, "Isolation and Properties of Bovine Kidney Brush Border Vacuolar H ⁺ -ATPase" J. Biol. Chem. 265(35):21957-21965.

NY02:42656	7.1			 .	
Examiner	S. J.	Date Considered	3	Mar 03	

^{*} Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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· N	OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)
60	Bowman EJ et al., 1988, "Bafilomycins: A class of inhibitors of membrane ATPases from microorganisms, animal cells, and plant cells" <i>Proc. Natl. Acad. Sci. USA</i> 85:7972-7976.
61. Galloway CJ et al., 1988, "Analysis of endosome and lysosome acidification in vitro" Med Enzymol. 157:601-611.	
62	Nelson N et al., 1988, "Chromaffin granule proton pump" Methods In Enzymol. 157:619-633.
63	Mains RE et al., 1988, "The role of a low pH intracellular compartment in the processing, storage, and secretion of ACTH and endorphin" J. Biol. Chem. 263(16):7887-7894.
64	Arai H et al., 1987, "Subunit composition and ATP site labeling of the coated vesicle proton-translocating adenosinetriphosphatase" Biochemistry 26:6632-6638.
65	Wu GY et al., 1987, "Receptor-mediated in vitro gene transformation by a soluble DNA carrier system" J. Biol. Chem. 262(10):4429-4432.
66	Anderson RGW et al., 1984, "Visualization of acidic organelles in intact cells by electron microscopy" Proc. Natl. Acad. Sci. USA 81:4838-4842.
67	Arvan P et al., 1984, "Osmotic properties and internal pH of isolated rat parotid secretory granules" J. Biol. Chem. 259(21):13567-13572.
68	Glickman J et al., 1983, "Golgi membranes contain an electrogenic H ⁺ pump in parallel to a chloride conductance" J. Cell Biol. <u>97</u> :1303-1308.
69	Revell SH, 1983, "Relationships between chromosome damage and cell death" Chromosome Damage and Cell Death pp. 215-233.
70	Seglen PO et al., 1981, "3-Methyladenine: Specific inhibitor of autophagic/lysosomal protein degradation in isolated rat hepatocytes" <i>Proc. Natl. Acad. Sci. USA</i> 79:1889-1892.
71	O'Farrell PH, 1975, "High resolution two-dimensional electrophoresis of proteins" J. Biol. Chem. 250(10):4007-4021.

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^{*} Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.